20 JM 1/10/03

Docket No.: 576-008

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
PATENT OPERATIONS

In re Application of:)
) Group Art Unit: 1641
Massimo Porro)
) Examiner:Minnifield, N.
Serial No.: 09/124,280)
Filed: July 29, 1998)

For: **VACCINES FOR PREVENTION OF GRAM-NEGATIVE INFECTIONS AND ENDOTOXIN RELATED DISEASE**

New York, NY 10036
December 30, 2002

Commissioner for Patents
Washington, DC 20231

APPEAL BRIEF

Sir:

This is an appeal from the final rejection of claims 1-8, 10-17, 19-34, 51, 54, 55 and 57-64.

(1) Real party in interest. The real party in interest is BioSynth S.r.l.

(2) Related appeals and interferences. There are no related appeals or interferences.

(3) Status of the claims. Claims 35, 37-50, 52 53 and 56 have been allowed. Claims 1-8, 10-17, 19-34, 51, 54, 55 and 57-64 have been finally rejected over the prior art.

(4) Status of amendments. There are no unentered amendments.

(5) Summary of invention. The invention is directed to a vaccine that is prepared by making an endotoxoid that is made by combining LPS free or in conjugate form with a stoichiometric excess of a peptide of the formula:

(a) $(A)_n$ wherein A is Lysine or Arginine and n is an integer with a minimum value of 7;
(b) $(AB)_m$ wherein A is Lysine or Arginine and B is a hydrophobic amino acid selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; m is an integer with a minimum value of 3; and (c) $(ABC)_p$ wherein A is a cationic amino acid which is Lysine or Arginine; B and C are hydrophobic amino acids which may be the same or different and are selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; p is an integer with a minimum value of 2.

(6) Issues.

Is the rejection of the claims as anticipated under 35 U.S.C.§102(b) a proper rejection?

(7) Grouping of claims. All of the claims may be grouped together for purposes of this appeal except claims 54, 63 and 64 which will be separately discussed.

(8) Argument.

Claims 1-8, 10-17, 19-34, 51, 54, 55 and 57-641-17, 19-34 and 51, which define a vaccine, were rejected under 35 U.S.C.§102(b) as being unpatentable over Porro (WO 95/03327). All of the claims to the process of making the vaccine have been rejected. In Paper No. 16, the Examiner stated:

> Applicant states that the prior art does not teach using a stoichiometric excess of peptide relative to the lipid moiety and that the method Applicant uses to make the vaccine is not disclosed in the prior art. However, the claimed invention is a vaccine comprising LPS and a peptide which the prior art discloses. Applicant appears to be arguing a process limitation and novel process or improved methods of preparing the vaccine, not the vaccine composition itself.

The claims at issue define a vaccine as a complex obtained

by combining LPS ... with a stoichiometric excess of a peptide. The applicant does not contend that the claims to the vaccine are free of a process limitation. The applicant's position is that the process limitation of the claims to the vaccine may be relied upon to point out a novel composition of matter that is not disclosed in the cited reference.

All of the finally rejected claims contain the recitation "a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide, on a weight basis relative to said LPS". The present specification, at page 6, lines 24-32 discloses that the vaccine is prepared by combining LPS with a peptide on specific weight/weight ratios. This language defines novel subject matter over the prior art description of making the vaccine disclosed in the Porro patent publication WO/95/03327 ('327 publication).

The '327 publication at page 7, lines 14-20 states that the vaccines may be made "using stoichiometric amounts of Lipid-A or LPS with the peptide". This does not disclose a vaccine having a "stoichiometric excess of peptide relative to the lipid moiety". In the absence of a disclosure of the presently claimed concept of using a stoichiometric excess of the peptide relative to LPS, it is submitted that the claims do not disclose a vaccine having a stoichiometric excess of a peptide relative to the LPS component. For this reason, the claims define novel subject matter and the rejection under 35 U.S.C.§102(b) should be reversed.

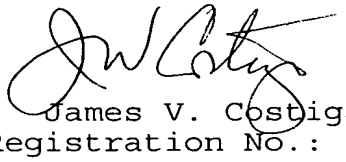
Claims 54 and 63 specify the stoichiometric excess as being a ratio of from 2 to 5000 units of peptide to one unit of LPS or 2 to 2500 units of peptide to one unit of LPS. Claim 64 specifies a ratio of 250 to 2500 of peptide to LPS. These ratios all define a novel vaccine as the prior art is limited to a 1:1 ratio of peptide to LPS.

MPEP §2113 is instructive regarding the manner in which a product-by-process claim is to be considered for patentability. Novelty of a product cannot be based on the novelty of the process. In the present case, the novelty of the product is not based on the novelty of the process. Novelty is predicated on the

presence of the stoichiometric excess of the peptide component of the vaccine. The Examiner has not cited any prior art that discloses a vaccine which has a stoichiometric excess of the peptides defined in the claims in combination with LPS. The claims do not include any vaccine suggested by the prior art which were explicitly described as being based on a one to one ratio of the peptide and LPS. The only issue raised in the final rejection was the novelty of the claims. It is submitted that the applicant has demonstrated that the claims are directed to novel vaccines and for this reason, the rejection under 35 U.S.C.§102(b) should be reversed.

The applicant has disclosed an advance in the useful art of making vaccines which meets the novelty requirements of the statute. For this reason, patent protection should be granted to promote the useful art of making vaccines.

Respectfully submitted,



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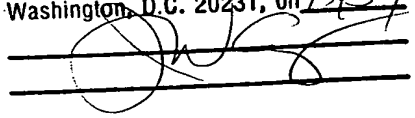

9. Appendix

Claims 1, 10-11, 19-24, 26-35, 37-41, 47, 49, 51, 54 and 55 as follows:

1. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide ,on a weight basis relative to said LPS, said peptide comprising:
(a) $(A)_n$ wherein A is Lysine or Arginine and n is an integer with a minimum value of 7;
(b) $(AB)_m$ wherein A is Lysine or Arginine and B is a hydrophobic amino acid selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; m is an integer with a minimum value of 3; and (c) $(ABC)_p$ wherein A is a cationic amino acid which is Lysine or Arginine; B and C are hydrophobic amino acids which may be the same or different and are selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; p is an integer with a minimum value of 2.

10. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide ,on a weight basis relative to said LPS wherein the peptide comprises: $(Lys\text{-}Phe)_5$ (SEQ ID NO: 5).

11. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises: Lys-Phe-Leu-Lys-Lys-Thr-Leu (SEQ ID NO: 6).

12. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

$(Lys\text{-}Phe\text{-}Leu)_2\text{-}Lys$ (SEQ ID NO: 7)

13. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:
$(Lys\text{-}Phe\text{-}Leu)_3\text{-}Lys$ (SEQ ID NO: 8)

14. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:
$(Arg\text{-}Tyr\text{-}Val)_3$ (SEQ ID NO: 9)

15. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:
$(Lys\text{-}Phe\text{-}Phe)_3\text{-}Lys$ (SEQ ID NO: 10)

16. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:
$(Lys\text{-}Leu\text{-}Leu)_3$ (SEQ ID NO: 11)

17. (twice amended) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:
$(Lys)_6(Phe\text{-}Lys)_2$ (SEQ ID NO: 12)

19. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Cys-Lys-Phe-Lys-Lys-Cys
s----------s (SEQ ID NO: 14)

20. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Lys-Phe-Lys-Cys-Lys-Phe-Lys-Phe-Lys-Cys
s----------s (SEQ ID NO: 15)

21. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Lys-Leu-Lys-Cys-Lys-Leu-Lys-Leu-Lys-Cys
s----------s (SEQ ID NO: 16)

22. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Arg-Thr-Arg-Cys-Arg-Phe-Lys-Arg-Arg-Cys
s----------s (SEQ ID NO: 17)

23. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide

comprises:

Lys-Cys-$(Lys\text{-}Phe\text{-}Lys)_2$-Cys-Lys

s----------s (SEQ ID NO: 18)

24. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Cys-$(Lys)_4$-$(Phe)_4$-Cys

s----------s (SEQ ID NO: 19).

26. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Val-Lys-Ala-Leu-Arg-Val-Arg-Arg-Leu (SEQ ID NO: 21).

27. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Lys-Ser-Leu-Ser-Leu-Lys-Arg-Leu-Thr-Tyr-Arg (SEQ ID NO:22).

28. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Lys-Val-Arg-Lys-Ser-Phe-Phe-Lys-Val (SEQ ID NO: 23).

29. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide

comprises:
Phe-Leu-Lys-Pro-Gly-Lys-Val-Lys-Val (SEQ ID NO: 24).

30. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:
Lys-Glu-Leu-Lys-Arg-Ile-Lys-Ile (SEQ ID No: 25)

31. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:
Lys-Trp-Lys-Ala-Gln-Lys-Arg-Phe-Leu (SEQ ID NO: 26)

32. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:
Lys-Trp-Lys-Ala-Gln-Lys-Arg-Phe-Leu-Lys (SEQ ID NO: 27)

33. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:
Lys-Arg-Leu-Lys-Trp-Lys-Tyr-Lys-Gly-Lys-Phe (SEQ ID NO:28)

34. A vaccine for preventing-gram negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

Lys-Thr-Lys-Cys-Lys-Phe-Leu-Lys-Lys-Cys(SEQ ID NO:31)
s - - - - - - - - - - - - s.

35. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

Cys-Lys-Phe-Leu-Lys-Lys-Cys
s----------s (Seq ID NO: 30).

37. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

Lys-Phe-Leu-Lys-Lys-Thr(SEQ ID NO: 32).

38. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

Cys-Lys-Lys-Leu-Phe-Lys-Cys-Lys-Thr-Lys
s - - - - - - - - - - - - s(SEQ ID NO: 33).

39. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

Cys-Lys-Lys-Leu-Phe-Lys-Cys-Lys-Thr
s - - - - - - - - - - - - s(SEQ ID NO: 34).

40. A vaccine for preventing gram-negative infections which

comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

Ile-Lys-Thr-Lys-Cys-Lys-Phe-Leu-Lys-Lys-Cys
s - - - - - - - - - - - s(SEQ ID NO: 35).

41. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

Ile-Lys-Thr-Lys-Lys-Phe-Leu-Lys-Lys-Thr(SEQ ID NO: 36).

47. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

$(Lys)_6$Phe-Leu-Phe-Leu(SEQ ID NO:42).

49. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

Lys-Trp-Lys-Ala-Gln-Lys-Arg-Phe-Leu-Lys(SEQ ID NO: 44).

51. A method for the preparation of a vaccine for prevention of gram-negative infections, said method comprising combining LPS with a stoichiometric excess of a peptide on a weight basis relative to said LPS comprising:

(a) $(A)_n$ wherein A is Lysine or Arginine and n is an integer with a minimum value of 7;

(b) $(AB)_m$ wherein A is Lysine or Arginine and B is a

hydrophobic amino acid selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; m is an integer with a minimum value of 3; and (c) $(ABC)_p$ wherein A is a cationic amino acid which is Lysine or Arginine; B and C are hydrophobic amino acids which may be the same or different and are selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; p is an integer with a minimum value of 2.

54. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of peptide:LPS where there is an excess of from 2 to 5000 times by weight of peptide, said peptide comprising:
(a) $(A)_n$ wherein A is Lysine or Arginine and n is an integer with a minimum value of 7;
(b) $(AB)_m$ wherein A is Lysine or Arginine and B is a hydrophobic amino acid selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; m is an integer with a minimum value of 3; and (c) $(ABC)_p$ wherein A is a cationic amino acid which is Lysine or Arginine; B and C are hydrophobic amino acids which may be the same or different and are selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; p is an integer with a minimum value of 2.

55. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS in a free form or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS of the formula:
Cys-$(Lys)_5$-Cys
s----------s (SEQ ID NO: 13)

57. A vaccine as defined in claim 1 wherein the LPS is derived from N. meningtidis, H. influenzae, Moraxella catharralis, Pseudomonas aeruginosa, Salmonella enterica and Escherichia

coli.

58. A vaccine as defined in claim 57 wherein the LPS is derived from Salmonella enterica.

59. A vaccine as defined in claim 57 wherein the LPS is derived from H. influenzae.

60. A vaccine as defined in claim 57 wherein the LPS is derived from N. meningtidis.

61. A vaccine as defined in claim 57 wherein the LPS is derived from Moraxella catharralis.

62. A vaccine as defined in claim 57 wherein the LPS is derived from Escherichia coli.

63. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of peptide:LPS where there is an excess of from 2 to 2500 times by weight of peptide, said peptide consisting essentially of:
(a) $(A)_n$ wherein A is Lysine or Arginine and n is an integer with a minimum value of 7;
(b) $(AB)_m$ wherein A is Lysine or Arginine and B is a hydrophobic amino acid selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; m is an integer with a minimum value of 3; and (c) $(ABC)_p$ wherein A is a cationic amino acid which is Lysine or Arginine; B and C are hydrophobic amino acids which may be the same or different and are selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; p is an integer with a minimum value of 2.

64. A vaccine for preventing gram-negative infections as defined in claim 63 which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric

excess of peptide:LPS where there is an excess of from 250 to 2500 times by weight of peptide.

Docket No.: 576-008

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
PATENT OPERATIONS

In re Application of:	Group Art Unit: 1641
Massimo Porro	Examiner:Minnifield, N.
Serial No.: 09/124,280	
Filed: July 29, 1998	

For: **VACCINES FOR PREVENTION OF GRAM-NEGATIVE INFECTIONS AND ENDOTOXIN RELATED DISEASE**

New York, NY 10036
December 30, 2002

Commissioner for Patents
Washington, DC 20231

LETTER

Sir:

Attached are three copies of an Appeal Brief and a Check for $160.00 in payment of the Appeal Fee.

Any additional fees may be charged to Deposit Account No. 08-1540.

Respectfully submitted,

James V. Costigan
Registration No.: 25,669

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:

Douglas T. Ross
Hansjorg Sauer
Gregory S. Hamilton
Joseph P. Steiner

Serial No.: 09/134,422

Filed: August 14, 1998

For: COMPOSITIONS AND USES FOR VISION AND MEMORY DISORDERS

Group Art Unit: 1623

Examiner: H. Owens, Jr.

Office Action mailed: 3/13/2001

BRIEF OF APPELLANT

I. Real Party in Interest

The present application is assigned to Guilford Pharmaceuticals Inc.

II. Related Appeals and Interferences

Other pending applications, that are currently on appeal to the Board of Patent Appeals and Interferences and may be considered to be related, include S.N. 09/134,472; S.N. 09/134,419; and S.N. 09/134,421.

III. Status of Claims

Claims 1-2 and 5-19 are the only claims pending in the application. All stand finally rejected.

IV. Status of Amendments

An amendment after final rejection was submitted on September 13, 2001, and was refused entry in the Office action dated October 19, 2001. The appended claims reflect entered amendments only.

V. Summary of Invention

The invention is a method for treating a nerve-related vision disorder or treating memory impairment. The method includes administering an effective amount of a non-immunosuppressive FKBP neuroimmunophilin ligand.

VI. Issues

A. Whether Claims 1-2 and 5-19 were improperly rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 12-16 of U.S. Patent No. 5,614,547?

B. Whether Claims 1-2 and 5-19 were improperly rejected under 35 U.S.C. § 103 as being unpatentable over U.S. Patent Nos. 5,614,547 and 5,847,449?

VII. Grouping of Claims

The claims stand or fall together.

VIII. Argument

A. Claims 1-2 and 5-19 were improperly rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 12-16 of U.S. Patent No. 5,614,547.

An obviousness-type double patenting rejection must establish that the present invention was merely an obvious variation of the subject matter defined by a claim in an issued patent. In re Braat, 937 F.2d 589, 592, 19 USPQ2d 1289, 1292 (Fed. Cir. 1991).

In the present case, the '547 patent claims use of a compound to treat certain disorders, and the appealed claims recite instead the treatment of vision disorders or memory impairment. According to the examiner, the motivation or suggestion to make the required changes and arrive at the invention of the appealed claims was that the '547 patent claims use of the compound to treat or effect neuronal activity, and therefore it would have been *per se* obvious to use the compound to treat any condition having a neurological basis:

> Given that the claims of '547 are drawn to treating or effecting neuronal activity via stimulation of damaged neurons, promotion of neuronal regulation and treatment of a neurological disorder using FKBP-type immunophillin ligands as set forth in the instant application, one of skill in the art would certainly have a reasonable expectation of success in the use of these compounds to treat conditions which have a neurological basis as well as be provided with the motivation to use these compounds for disorders which have a neurological etiology or constitute neuronal degeneration.

Final rejection dated March 13, 2001, page 3. Such a *per se* rejection fails to establish the required motivation or suggestion in the prior art. There is no evidence of record that

one of ordinary skill in the art expected a compound effective for certain neurological disorders to be effective for every other neurological disorder, or for vision disorders or memory impairment.

Because the examiner's *per se* rejection does not set forth a *prima facie* case of obviousness, the Board need not consider the rebuttal evidence submitted by Appellants. However, if the examiner were to provide *prima facie* evidence that a compound useful in treating certain neurological disorders was expected successfully to treat every other neurological disorder, it would be rebutted by the evidence that is of record.

The record reflects that compounds such as Imipramine used for treating symptoms associated with Alzheimer's Disease are not effective for treating memory impairment, and there is also no expectation that such compounds would be effective in treating vision disorders. Teri et al., J. Gerontology, 46 (1991) 372-377 (copy attached as Addendum A). In fact, the researchers postulate that higher dosages of Imipramine effective for treating depression associated with Alzheimer's Disease may actually affect cognition adversely. Id. at 376. However, since the examiner has not even attempted to relate the '547 patent claims to the specific disorders recited in the appealed claims, the rejection may be reversed on that basis alone.

B. Claims 1-2 and 5-19 were improperly rejected under 35 U.S.C. § 103 as being unpatentable over U.S. Patent Nos. 5,614,547 and 5,847,449.

The § 103 rejection over the combined teachings of the '547 patent and the '449 patent should be reversed for the same reasons stated above with respect to the

obviousness-type double patenting rejection and for the following additional reasons. The only motivation or suggestion identified by the examiner is that the references teach treatment of neurological disorders:

> A person of ordinary skill in the art would have been motivated to use the analogous compounds for the treatment of nerve related vision disorders or memory impairments given the general use of these compounds in the prior art for stimulation of damaged neurons, promotion of neuronal regulation and treatment of neurological disorders; as well as the non-immunosuppressive activity displayed by these compounds.

Final rejection dated March 13, 2001, page 5. The prior art's treatment of some neurological disorders does not suggest that the recited compound would work for any and every other neurological disorder.

Moreover, nothing in any of the references mentions the specific conditions recited in the present claims, let alone suggests treating them with the recited compound. The examiner asserts that the '449 patent teaches "treatment of memory impairment such as Alzheimer's disease." That assertion is factually incorrect. Alzheimer's Disease is not a type of memory impairment, and nothing in the cited references suggests that it is. In fact, nothing in any cited reference even mentions memory.

There is no evidence of record that a compound useful for Alzheimer's Disease, Parkinson's Disease, and the other conditions mentioned in the cited references was

expected to work for vision disorders or memory impairment. Without such evidence, the rejection must fail:

> With respect to core factual findings in a determination of patentability, however, the Board cannot simply reach conclusions based on its own understanding or experience—or on its assessment of what would be basic knowledge or common sense.

In re Zurko, 238 F. 3d 1379, 1385-86, 59 USPQ2d 1693, 1697 (Fed. Cir. 2001); In re Lee, Appeal No. 00-1158, 61 USPQ2d 1430, 1435 (Fed. Cir. Jan. 18, 2002).

The examiner may have some personal unstated understanding regarding a relationship between Alzheimer's Disease and memory impairment. However, the examiner provides no evidence regarding such relationship. No cited reference mentions memory impairment. No cited reference mentions vision disorders. Lacking evidence, the rejection is improper under Zurko and Lee.

Because the rejection does not establish a *prima facie* case of obviousness, the Board need not consider the rebuttal evidence submitted by Appellants. However, if the examiner were to provide *prima facie* evidence that a compound useful in treating certain neurological disorders was expected successfully to treat vision disorders or memory impairments, it would be rebutted by the evidence that is of record. The record reflects that compounds such as Imipramine used for treating symptoms associated with Alzheimer's Disease are not effective for treating memory impairment, and there is also no expectation that such compounds would be effective in treating vision disorders. Teri et al., J. Gerontology, 46 (1991) 372-377 (copy attached as Addendum A). In fact, the

researchers postulate that higher dosages of Imipramine effective for treating depression associated with Alzheimer's Disease may actually affect cognition adversely. Id. at 376.

IX. Conclusion

The rejections of Claims 1-2 and 5-19 should be reversed for the reasons stated.

For the Appellant:

LYON & LYON LLP

Dated: April 2, 2002

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CLAIMS

1. *(Twice amended)* A method for treating a nerve-related vision disorder, improving vision, treating memory impairment or enhancing memory performance in a mammal in need thereof, which comprises administering to said animal an effective amount of a non-immunosuppressive FKBP neuroimmunophilin ligand, wherein the nerve-related vision disorder is selected from the group consisting of visual impairments; orbital disorders; disorders of the lacrimal apparatus; disorders of the eyelids; disorders of the conjunctiva; disorders of the cornea; cataract; disorders of the uveal tract; disorders of the retina; disorders of the optic nerve or visual pathways; free radical induced eye disorders and diseases; immunologically-mediated eye disorders and diseases; eye injuries; and symptoms and complications of eye disease, eye disorder, and eye injury.

2. The method of claim 1, wherein the FKBP neuroimmunophilin is FKBP-12.

5. The method of claim 1, wherein the nerve-related vision disorder is retinal ischemia.

6. The method of claim 5, wherein the retinal ischemia is selected from the group consisting of degeneration of retinal ganglion cells, degeneration of optic nerve axons, degeneration of myelin sheaths, ischemic optic neuropathy, and retinal vascular blockage.

7. The method of claim 1, wherein the nerve-related vision disorder is optic nerve transection.

8. The method of claim 7, wherein the optic nerve transection is selected from the group consisting of ganglion cell death after optic nerve transection and myelin degeneration after optic nerve transection.

9. The method of claim 1, wherein the nerve-related vision disorder is diabetes.

10. The method of claim 9, wherein the diabetes is selected from the group consisting of diabetes from degeneration and diabetic retinopathy.

11. The method of claim 1, wherein the nerve-related vision disorder is macular degeneration.

12. The method of claim 1, wherein the nerve-related vision disorder is glaucoma related degeneration.

13. The method of claim 1, wherein the nerve-related vision disorder is cataract related degeneration.

14. The method of claim 1, wherein the nerve-related vision disorder is a detached retina.

15. The method of claim 1, wherein the nerve-related vision disorder is inflammation related degeneration.

16. The method of claim 1, wherein the nerve-related vision disorder is photoreceptor degeneration.

17. The method of claim 1, wherein the nerve-related vision disorder is optic neuritis.

18. The method of claim 1, wherein the nerve-related vision disorder is dry eye degeneration.

19. The method of claim 1, wherein the mammal is human.